

# VU Research Portal

## Internet-Delivered Cognitive Behavioral Therapy for Insomnia

van der Zweerde, T.; Lancee, Jaap; Ida Luik, Annemarie; van Straten, Annemieke

### **published in**

Sleep Medicine Clinics  
2019

### **DOI (link to publisher)**

[10.1016/j.jsmc.2019.04.002](https://doi.org/10.1016/j.jsmc.2019.04.002)

### **document version**

Publisher's PDF, also known as Version of record

### **document license**

Article 25fa Dutch Copyright Act

[Link to publication in VU Research Portal](#)

### **citation for published version (APA)**

van der Zweerde, T., Lancee, J., Ida Luik, A., & van Straten, A. (2019). Internet-Delivered Cognitive Behavioral Therapy for Insomnia: Tailoring Cognitive Behavioral Therapy for Insomnia for Patients with Chronic Insomnia. *Sleep Medicine Clinics*, 14(3), 301-315. <https://doi.org/10.1016/j.jsmc.2019.04.002>

### **General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

### **Take down policy**

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

### **E-mail address:**

[vuresearchportal.ub@vu.nl](mailto:vuresearchportal.ub@vu.nl)

# Internet-Delivered Cognitive Behavioral Therapy for Insomnia

## Tailoring Cognitive Behavioral Therapy for Insomnia for Patients with Chronic Insomnia



Tanja van der Zweerde, MSc<sup>a,\*</sup>, Jaap Lancee, PhD<sup>b,c</sup>,  
Annemarie Ida Luik, PhD<sup>d</sup>, Annemieke van Straten, PhD<sup>a</sup>

### KEYWORDS

- Chronic insomnia • Insomnia • Internet • Cognitive behavioral therapy (CBT)
- CBT for Insomnia (CBTI) • Online psychological treatment • Tailoring treatment

### KEY POINTS

- Insomnia is an important public health issue with high prevalence, disease burden, and economic costs. Insomnia is preferably treated with cognitive behavioral therapy (CBTI).
- Both face-to-face and Internet-delivered CBT for Insomnia (I-CBTI) are evidence-based effective treatments.
- I-CBTI has yet to reach its full potential in both scope and scale. More developments toward improved effectiveness could further improve I-CBTI.
- I-CBTI can be successfully offered to a wide and varied range of insomnia sufferers and is suggested to be effective irrespective of demographic variation or baseline severity.
- Research should focus on working mechanisms and moderators of effects, aimed at implementation of tailored Internet treatments to successfully treat more people.

### PRECISION MEDICINE FOR INSOMNIA DISORDER

Insomnia is a common mental disorder, characterized by complaints of dissatisfaction with sleep quantity, sleep quality, or both. Persons with insomnia suffer from these symptoms 3 or more

nights per week, for at least 3 months, which results in significant distress or impaired daytime functioning (*Diagnostic and Statistical Manual of Mental Disorders, 5th Edition: DSM-5*<sup>1</sup>; for full criteria see [Table 1](#)). Approximately one-third of the population suffers from occasional insomnia symptoms, whereas approximately 7% to 10% fit

**Disclosure Statement:** The online cognitive behavioral therapy for insomnia program, i-Sleep, was developed at the VU University Amsterdam by Annemieke van Straten and further developed in collaboration with Jaap Lancee (University of Amsterdam) and T. van der Zweerde (VU University). The authors have no commercial interest in this program. Annemarie Luik has previously worked in a position funded by Big Health Inc. (Sleepio); she currently has no commercial or financial interest in Big Health Inc.

<sup>a</sup> Department of Clinical Psychology, EMGO Institute for Health and Care Research, VU University, Van der Boerhorststraat 7, Amsterdam 1081 BT, the Netherlands; <sup>b</sup> Department of Clinical Psychology, University of Amsterdam, Nieuwe Achtergracht 129, Amsterdam 1018 WS, the Netherlands; <sup>c</sup> PsyQ Amsterdam, Amsterdam, the Netherlands; <sup>d</sup> Department of Epidemiology, Erasmus MC University Medical Center, Dr. Molewaterplein 40, Rotterdam 3015 GD, the Netherlands

\* Corresponding author.

E-mail address: [t.vander.zweerde@vu.nl](mailto:t.vander.zweerde@vu.nl)

Sleep Med Clin 14 (2019) 301–315

<https://doi.org/10.1016/j.jsmc.2019.04.002>

1556-407X/19/© 2019 Elsevier Inc. All rights reserved.

**Table 1**  
**DSM-5 and ICSD-3 diagnosis of insomnia disorder**

Classification System	Duration	Frequency	Sleep Complaints
DSM-5	≥3 mo	≥3 nights per week	Difficulty initiating sleep, maintaining sleep, and/or early morning awakening with inability to return to sleep despite adequate opportunity for sleep. Resulting in significant impairment of daytime functioning and/or significant distress. Not better explained by another sleep-wake disorder, physiologic effects of substances or coexistent conditions.
ICSD-3	≥3 mo	≥3 nights per week	Difficulty initiating sleep, maintaining sleep, waking up earlier than desired, resistance to going to bed at appropriate time, and/or difficulty sleeping without intervention. Fatigue/malaise, impaired attention/concentration/memory, impaired performance (social, familial, occupational, or academic), mood disturbance/irritability, daytime sleepiness, behavioral problems (eg, hyperactivity, impulsivity, or aggression), reduced motivation/energy/initiative, proneness to judgment errors or to physical accidents, and/or concerns about or dissatisfaction with sleep. Reported sleep-wake complaints cannot be explained purely by inadequate opportunity or circumstance for sleep: enough time has been allotted for sleep and the environment is safe, dark, quiet, and comfortable. Sleep-wake difficulty is not better explained by another sleep disorder (intoxication and acute withdrawal are ruled out).

*Abbreviations:* DSM-5, diagnostic and statistical manual of mental disorders, 5th Edition: DSM-5; ICSD-3, international classification of sleep disorders. Third Edition.

clinical criteria for an insomnia diagnosis.<sup>2,3</sup> People typically suffer from insomnia for multiple years<sup>3</sup> before diagnosis. Insomnia also increases the risk for other mental and physical health problems, and persons with insomnia often develop comorbid mental health problems, such as depression or anxiety.<sup>4–6</sup> The economic burden of insomnia is considerable: poor sleepers cost society up to 10 times as much as good sleepers.<sup>7,8</sup> The high prevalence, costs, burden, and risk of insomnia warrant efficacious treatment. Precision medicine offers the potential to realize the best use of limited time and resources in (mental) health care. Internet-delivered therapy can facilitate a precision medicine approach, as components, intensity, order, reminders, and guidance can be tailored to suit the specific needs of the patient, but at the same time needs fewer resources than face-to-face solutions for precision medicine.

**COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA**

Currently, many people seeking help for insomnia are prescribed a pharmacologic treatment, mostly benzodiazepines or benzodiazepine receptor agonists (the so-called “Z-drugs”: zolpidem, zopiclone, zaleplon<sup>9</sup>). As short-term treatment, pharmacotherapies are effective in relieving insomnia<sup>10–12</sup>; however, pharmacotherapy has negative side effects,

such as headaches, drowsiness and dizziness, can alter sleep microstructure, and potentially leads to dependency and addiction when used long-term.<sup>11–13</sup> When a person quits medication, the person can also suffer from rebound effects.<sup>14</sup> Furthermore, the evidence for longer-term effects of pharmacotherapies is limited.<sup>15–17</sup> Despite these concerns, in the United States, use of prescription sleep aids has increased in recent years.<sup>10</sup> Other psychoactive medications such as antidepressants or antipsychotics are also used to treat insomnia, even though their effectiveness has not adequately been demonstrated in clinical trials.<sup>18</sup>

Fortunately, evidence-based alternatives to pharmacotherapy for persons with insomnia are available. Since the 1990s, a collection of different treatment components (educational, behavioral, and cognitive) has been offered as a combined treatment: cognitive behavioral therapy for insomnia (CBTI). An overview of the different components of CBTI is listed in [Table 2](#).<sup>21</sup>

Multiple reviews have concluded that CBTI is effective and has effects that last longer than those of pharmacologic treatments for insomnia. As a result, CBTI has a substantial evidence base for the treatment of insomnia.<sup>16,22–29</sup> Large posttreatment effects are reported on insomnia severity (Hedges ’g = 0.98), self-rated sleep efficiency (g = 0.71) and sleep quality (g = 0.65<sup>29</sup>). A recent meta-analysis<sup>30</sup> demonstrated that CBTI has

**Table 2**  
**Core cognitive behavioral therapy for insomnia components**

Component	Content
Psycho-education	Information about the process and function of normal and disturbed sleep.
Sleep hygiene and lifestyle advice	Information about a healthy lifestyle that can promote sleep (eg, low caffeine and alcohol intake), about behaviors and habits that hinder sleep, about adjustments that can be made to improve their sleep (eg, a suitable bedroom and bedtime routine). Fixed hours are set for bed and rising times aiming to stabilize the circadian rhythm.
Stimulus control	Person's associations between bed and sleep are reaffirmed by advice to get out of bed when awake >15 min, and only go back to bed when sleepy. The bed is to be used for sleep and sexual activity only.
Sleep restriction therapy	Person's time in bed is restricted to the average time a patient slept the past week (typically with a minimum of 5 hours). This heightens the homeostatic sleep drive (ie, patients are more tired), making them fall asleep easier and strengthens the bed-sleep association. When this results in less fragmented sleep, the sleep window is elongated slowly (see Refs. <sup>19,20</sup> ).
Relaxation techniques	Different relaxation and breathing exercises are used to teach patients to unwind and take more breaks during the day, for example, progressive muscle relaxation or meditation exercises.
Cognitive restructuring	Persons identify and challenge misconceptions (such as "I have to sleep 8 h a night") and worries that keep them awake. These might be related to sleep or to other non-sleep-related issues. Unhelpful thoughts are unpacked and challenged using cognitive techniques, such as gathering evidence for and against a certain belief or statement, and gathering evidence for a more helpful alternative.

positive long-term effects that last up to a year, showing an effect of clinically significant magnitude. Because of these favorable effects, international guidelines recommend CBTI as a first-line treatment rather than prescribing medication, or combining the 2 modalities if necessary.<sup>31,32</sup>

### **Online Cognitive Behavioral Therapy for Insomnia**

Although CBTI is recommended therapy for insomnia, many patients with insomnia do not receive CBTI. Several important reasons for this discrepancy can be identified. First, estimates are that only 50% of persons with insomnia actively seek help.<sup>33</sup> Second, given the high prevalence of insomnia<sup>2</sup> and the relatively small number of trained CBTI therapists, there is a discrepancy between the demand for treatment and available resources. Moreover, health care budgets are not sufficient to provide face-to-face CBT to everyone, even if therapists were available.

Third, general practitioners (GPs), often the first point of contact for persons with insomnia who seek treatment, rarely refer to psychological treatments for insomnia.<sup>34</sup>

As a potential solution to some of these issues CBTI could be offered in an online format (I-CBTI). Because I-CBTI requires less therapist input than face-to-face therapy, the same number of therapists can treat many more people. Furthermore, I-CBTI might be less stigmatizing and more easily accessible to patients. Going to a health care professional, such as a GP, is required in most cases to obtain access to online treatment, but patients may nonetheless regard this as a smaller and more easily accomplished step than being referred to mental health care facilities for help.

CBTI in an online format is similar to CBTI delivered face-to-face, containing mostly the same elements in the same order. Typically, I-CBTI is offered through secured Web sites that include informative texts, videos, graphs, and illustrations.

Participants provide information to the program via (interactive) questionnaires and a sleep diary. Many variations of I-CBTi exist, including variations that (1) use a mix of face-to-face sessions and I-CBTi, (2) use support and feedback from a health care professional, and (3) use fully automated support and feedback, either personalized or not. In most treatments, the number of sessions and their order is fixed, but some programs have opt-in elements in which participants can select components that they feel are relevant for them,<sup>35</sup> or provide a mix of fixed and optional components.<sup>36</sup>

### **EFFICACY OF INTERNET-DELIVERED COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA**

In 2004, Ström and colleagues<sup>37</sup> published the first randomized controlled study investigating Internet-based treatment for insomnia. Since then, many more studies and digital programs for insomnia have been developed. To our knowledge, 13 different I-CBTi programs have been studied in a randomized controlled trial (Refs.<sup>35–49</sup>; **Table 3**), of which most programs were developed for adults except 1 program for adolescents.<sup>49</sup> Although the number of online treatments for insomnia is expected to continue to grow rapidly, only a small percentage has been evidence-based so far, leaving many more programs without any evidence base accompanied by unknown efficacy and risks, potentially even causing harm.

### **GUIDANCE IN ONLINE COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA PROGRAMS**

Most programs offer at least some form of therapeutic guidance, either automated or by a therapist, that is, human feedback. Common elements are feedback on sleep diaries that a person keeps, as well as motivational messages to help participants adhere to the program, and providing additional instructions and explanations when necessary. Participants usually receive online feedback and motivational support for every session they complete. Providing human feedback takes an estimated 15 to 30 minutes per online participant per session and can be provided by psychologists, other health care professionals, or by clinical psychology students.<sup>36,52,54,57</sup> Automated feedback also is used.<sup>35,39,48</sup> Extensive programming ensures that participants receive tailored messages suited to their situation and sleep patterns.

Research on online treatments for other psychological disorders reports that support promotes adherence and increases effects<sup>58</sup>; however, only 2 studies have investigated these effects in online insomnia treatment. Both report that support, even if it is very limited, improves effectiveness.<sup>59,60</sup> More research is needed to identify the optimal form and dosage of support. If I-CBTi is to offer a true alternative to pharmacotherapy and be implemented on a large scale, personal (online) support or guidance could present a challenge. Current and future developments not yet applied to I-CBTi could be used to enhance automated support and guidance, for example, by using avatars and/or artificial intelligence.

### **EFFECTS OF INTERNET-DELIVERED COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA** *Effects on Insomnia of Internet-Delivered Cognitive Behavioral Therapy for Insomnia*

---

Overall, I-CBTi is effective and effect sizes seem in the same range as those of face-to-face treatments,<sup>61</sup> in line with research in, for example, Internet treatment for depression.<sup>62</sup> As such, it is suggested to be a viable treatment option. Since the meta-analysis by Zachariae and colleagues,<sup>61</sup> many trials have been published investigating an existing I-CBTi program (eg, Refs.<sup>35–46,48,50–54,56,57,59,63–67</sup>), and new programs have been introduced (eg, Refs.<sup>45,47</sup>). These studies reliably show positive effects (see **Table 3**).

The few direct comparisons that have been made between online and face-to-face CBTi have reported mixed results. Lancee and colleagues<sup>52</sup> found that face-to-face therapy substantially outperformed its online alternative. Blom and colleagues<sup>36</sup> compared I-CBTi with group therapy and did not report differences in effects. More research directly comparing face-to-face CBTi with I-CBTi is needed to compare effects of different treatment modalities and their moderators.

### *Effects of Internet-Delivered Cognitive Behavioral Therapy for Insomnia on Other (Mental) Health Symptoms and Daily Functioning*

---

Insomnia is often comorbid with psychological complaints. Insomnia plays a role in the onset of anxiety disorders, bipolar disorders, and suicidality, but is most notably related to depression.<sup>68</sup> Patients suffering from a major depressive episode have an 80% chance of also reporting insomnia symptoms.<sup>2</sup> In addition, a person suffering from insomnia is at greater risk for depression.<sup>69</sup>

**Table 3**  
**Different Internet-delivered cognitive behavioral therapy for insomnia (all components) programs studied**

Study	Program	Population	Scheduled Sessions	Support	Delivery	Indications of Effect Size <sup>a</sup>
Ström et al, <sup>37</sup> 2004	—	Adults	Order fixed, structured program at patients own <sup>b</sup> pace (5 sessions/wk)	Automated	Text-based	BAASS = 0.81. <sup>37</sup>
Suzuki et al, <sup>35</sup> 2008	—	Adults	Patients pick any 3 or more (4 sessions/2 wk)	Automated	Interactive Web platform	0.09–0.33 for SOL, TST, and SE. <sup>35</sup>
Vincent & Lewycky, <sup>38</sup> 2009	—	Adults	Fixed, structured program at patients own pace (5 sessions/6 wk)	None	Interactive Web platform	Range 0.14–0.75 for sleep diary variables. <sup>38</sup>
Espie et al, <sup>39</sup> 2012	Sleepio	Adults	Fixed, structured program at patients own pace (6 sessions/6 wk)	Automated, personalized	Interactive, virtual therapist	SCI = 0.89 <sup>50</sup> ; SCI = 1.11. <sup>51</sup>
Lancee et al, <sup>40</sup> 2012	—	Adults	Fixed, structured program at patients own pace (6 sessions)	None	Text-based	ISI = 1.00 <sup>52</sup> ; 1.05 <sup>43</sup> ; SLEEP50 Insomnia = 1.44 <sup>40</sup>
Ho et al, <sup>41</sup> 2014	—	Adults	Fixed, structured program at patients own pace (6 sessions/6 wk)	Weekly phone support vs no support	Interactive Web platform	ISI = 0.53 <sup>41</sup>
Van Straten et al, <sup>42</sup> 2014	I-Sleep	Adults	Fixed, structured program at patients own pace (text-based: 6 <sup>42</sup> ; interactive: 5, <sup>53</sup> over 5–8 wk).	Weekly personal online therapist support	Text-based <sup>42</sup> ; updated to interactive Web platform <sup>53</sup>	PSQI = 1.06 <sup>42</sup> ; ISI 2.36 <sup>53</sup>

(continued on next page)

**Table 3**  
(continued)

Study	Program	Population	Scheduled Sessions	Support	Delivery	Indications of Effect Size <sup>a</sup>
Blom et al, <sup>36</sup> 2015	—	Adults	Some elements fixed, some optional (8 sessions over 8 wk).	Weekly personal online therapist support	Text-based	ISI = 0.85 <sup>54</sup> , 1.8 <sup>36</sup>
Thiart et al, <sup>44</sup> 2016	Get.On Recovery	Adults	Fixed, structured program at patients own pace (6 sessions)	Weekly personal online therapist support	Interactive Web platform	ISI = 1.45 <sup>55</sup>
Bernstein et al, <sup>45</sup> 2017	GO! To sleep	Adults	Fixed, structured program at patients own pace (6 sessions/ 6 wk)	None	Interactive Web platform	n/a
Horsch et al, <sup>47</sup> 2017	Sleepcare	Adults	Fixed, structured program at patients own pace (6–7 wk)	Automated, personalized	Fully automated interactive app	ISI = 0.66 <sup>47</sup>
Hagatun et al, <sup>46</sup> 2017; Ritterband et al, <sup>48</sup> 2017	SHUT-I	Adults	Fixed, structured program at patients own pace (6 sessions/ 6 wk)	Automated, personalized	Interactive Web platform	ISI = 1.14 <sup>56</sup>
de Bruin et al, <sup>49</sup> 2015	—	Adolescents	Fixed weekly online sessions (6 sessions/6 wk)	Weekly personal feedback from a coach or therapist	Text-based	HSDQ insomnia scale = 1.26 <sup>49</sup>

**Abbreviations:** BAASS, beliefs and attitudes about sleep scale; C-E, cost-effectiveness; ES, effect size; HSDQ, Holland sleep disorder questionnaire; ISI, insomnia severity index; n/a, not available; P HQ-9, patient health questionnaire-9; PSQI, Pittsburgh sleep quality index; SCI, sleep condition indicator; SE, sleep efficiency; SOL, sleep onset latency; TST, total sleep time; —, no specific title for this program.

<sup>a</sup> Between-group (cognitive behavioral therapy for insomnia vs placebo, wait list, or no treatment) Cohen's *d* reported from publications when available; reported effect sizes are between-group unless otherwise indicated; this is a selection of studies and not an exhaustive overview. For programs with more than 3 randomized controlled trials (RCTs) available, the effect sizes of the most recent 3 RCTs were reported. Reporting on insomnia severity measure when available; sleep diary otherwise; and different measure if neither are available.

<sup>b</sup> Patient-paced programs commonly have a 1 week per session minimum.



Residual insomnia complaints after successful depression treatment also predict depression relapse.<sup>70</sup>

Similar to face-to-face CBTI,<sup>71,72</sup> I-CBTI also has been shown to have antidepressant effects.<sup>73</sup> Most participants studied in these meta-analyses,<sup>72,73</sup> however, were not recruited for depression specifically, and severely depressed persons were not included in these studies. Three recent I-CBTI studies specifically assessing I-CBTI as a treatment for depressive symptoms and insomnia showed promising results. Blom and colleagues<sup>57</sup> found I-CBTI to be more effective than online depression treatment on insomnia and equally effective on depressive symptoms. Christensen and colleagues<sup>64</sup> and van der Zweerde and colleagues<sup>53</sup> demonstrated that I-CBTI reduced both depressive symptoms and insomnia symptoms in people suffering from both.<sup>53,64</sup>

Depressive symptoms are not the only psychiatric complaints influenced by I-CBTI. A large study by Freeman and colleagues<sup>51</sup> on 3755 students showed that I-CBTI also leads to positive changes in psychotic symptoms. Improving insomnia has been suggested to have beneficial effects on other aspects of (mental) health and quality of life as well.<sup>50</sup> This is particularly important because daytime complaints and impaired daily functioning are often the reason to seek treatment.<sup>74</sup> There is also evidence of I-CBTI improving work performance and cognitive complaints.<sup>50,65,66</sup>

## FACTORS INFLUENCING INTERNET-DELIVERED COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA EFFECTS

Even though CBTI treatments are effective overall, the treatment does not work for everyone, up to an estimated 30% of persons with insomnia do not respond to treatment.<sup>75</sup> Why this is the case and which factors (eg, genetic, environmental, biological, lifestyle) play a role here is largely unknown. More research is needed to enable precision medicine approaches taking into account specific patient characteristics that influence the changes of treatment success.

Clear mediators and moderators of I-CBTI effects have yet to be determined. Some influential variables have been suggested by earlier research on CBTI (Table 4). It is yet unclear whether these factors differ between CBTI and I-CBTI, but it seems likely that comparable processes play a role in both treatment modalities.

### **Cognitive and Behavioral Factors**

The importance of cognitive processes in insomnia treatment has been well documented

over the past 20 years (eg, Refs.<sup>92–94</sup>). Cognitive processes, such as worrying and dysfunctional beliefs, have been studied as mediators of the effects of CBTI treatment, with varying results.<sup>43,56,76–80</sup> Overall, although not all studies study the same specific outcomes and cognitive processes, cognitive factors do seem to play a role. Two important factors worth mentioning are insomnia-related worrying and dysfunctional beliefs.<sup>81,95</sup> Harvey<sup>81</sup> suggests patients with insomnia perceive worrying to be beneficial to them (which may in itself be seen as a dysfunctional belief). At the same time, worrying also heightens arousal, making sleeping difficult. Dysfunctional beliefs (eg, “Without a good night’s rest I will not be able to function at work tomorrow”) are a topic of worry, and can also aggravate the perceived consequences of poor sleep.

Behavioral factors such as habits incompatible with sleep, varying bedtimes, and spending too much time in bed are commonly seen among bad sleepers and influence effects of treatment. Harvey and colleagues<sup>78</sup> recently concluded that the effects of these behavioral factors depend on the type of treatment (behavioral treatment [BT], cognitive therapy [CT], or a combination) a person undergoes.<sup>78</sup> They observed that behavioral processes mediated the results for BT but not for CT. Notably, the cognitive mediators studied (worry, unhelpful beliefs about sleep, and monitoring behavior for sleep-related threat) were significant mediators of the effect of BT as well as CT. When patients report a high level of disturbance in both behavioral and cognitive sleep-related processes, they achieved better treatment results when they received the combined CBT.<sup>78</sup>

### **Delivery-Mode-Specific Factors**

Online delivery may not be suited for everyone suffering from insomnia. Blom and colleagues<sup>86</sup> looked at patient-reported factors that facilitate and hinder uptake of I-CBTI. They found that having more than one psychological problem next to insomnia makes it more difficult to adhere to an I-CBTI program and may warrant different delivery modes or more intensive (human) support. A review on Internet therapy aimed at behavior changes emphasized that the intensity of a program should be high and that reminders, preferably text-messages, are important tools to enhance adherence.<sup>88</sup>

### **Sleep as a Perpetuating Factor in Other Psychiatric Problems**

Disturbed sleep is seen in 60% of psychiatric patients,<sup>96</sup> and is often a perpetuating factor, for



**Table 4**  
**Factors that have been suggested to play a role in precision medicine for insomnia**

Factors	Characteristic	Supported on Sequence	Level of Research Support
Mediators	Type of problem (cognitive or behavioral)	BT for primarily behavioral problems, CT for primarily cognitive problems, combined CBT when both are present.	<ul style="list-style-type: none"><li>• Empirical results on cognitive process vary,<sup>43,56,76–80</sup> their influence remains unclear.</li><li>• Empirical evidence does show insomnia-related worrying and dysfunctional beliefs about sleep mediate treatment effects.<sup>81</sup></li><li>• Behavioral processes mediated results for BT, but not for CT in RCT.<sup>78</sup></li></ul>
Predictors of treatment effects			
Demographic <sup>a</sup>	Age	Higher chance of treatment success with younger age.	<ul style="list-style-type: none"><li>• Meta-analytic evidence based on data from 49 studies.<sup>82</sup></li><li>• However: no evidence from older populations, age range in 90% of studies is quite small.<sup>82</sup></li></ul>
	Educational level	Higher chance of treatment success with higher educational level.	<ul style="list-style-type: none"><li>• Observational study of intervention group only (Vincent et al, 2001) showed education moderated effects.<sup>83</sup></li><li>• Not found to moderate effects in meta-analysis.<sup>82</sup></li></ul>
Clinical	Higher (>6 h) initial total sleep time <sup>b</sup>	Risk of dropout.	<ul style="list-style-type: none"><li>• Empirical evidence higher TST predicts dropout from dropped-out participants in RCT.<sup>84</sup></li></ul>
	Lower initial total sleep time (<6 hr)	Lower chance of treatment success.	<ul style="list-style-type: none"><li>• Empirical evidence from RCT results.<sup>85</sup></li></ul>
	Lower initial insomnia severity	Lower change of treatment success, may predict dropout.	<ul style="list-style-type: none"><li>• Empirical evidence from dropped-out participants in RCT.<sup>84</sup></li></ul>
	Higher initial sleep efficiency <sup>b</sup>	Lower chance of treatment success.	<ul style="list-style-type: none"><li>• Suggested in 2014 conference abstract, results not published to our knowledge.<sup>83</sup></li></ul>
	Other sleep disorders	Lower chance of treatment success.	<ul style="list-style-type: none"><li>• Observational study of intervention group only (Vincent et al, 2001) showed sleep comorbidity moderated effects.<sup>83</sup></li></ul>
	Other psychiatric or medical disorders	Chance of lower adherence.	<ul style="list-style-type: none"><li>• Empirical RCT evidence shows psychiatric comorbidities warrant more intensive delivery modes/ more intensive (human) support/scheduled program reminders.</li></ul>

(continued on next page)

Table 4  
(continued)

Factors	Characteristic	Supported on Sequence	Level of Research Support
			<ul style="list-style-type: none"><li>• Meta-analytic evidence of effect sizes equal to effect sizes in non-comorbid samples.<sup>73</sup></li><li>• Psychiatric comorbidities do not seem to decrease treatment effects and comorbidities may benefit from CBTi as well.<sup>53,57,64,86–88</sup></li><li>• Meta-analytic evidence shows the positive response to CBTi on insomnia symptoms does not appear to be moderated by the type of comorbid condition (psychiatric/medical).<sup>89</sup></li></ul>
	Insomnia subtype	Different treatment (elements) may be indicated depending on for example, level of distress.	Insomnia subtypes identified by Blanken and colleagues, <sup>90</sup> further research and clinical application needed.

Abbreviations: BT, behavioral therapy; CBTi, cognitive behavioral therapy for insomnia; CT, cognitive therapy; RCT, randomized controlled trial; TST, total sleep time.

<sup>a</sup> Research suggests only 2.2% of variance in CBTi treatment effects on sleep efficiency (SE) was due to demographics (conference abstract by Espie and colleagues,<sup>83</sup> 2014).

<sup>b</sup> Paradoxical insomnia could also play a role when TST and/or SE are high but patients experience an insomnia problem nonetheless.<sup>91</sup>

example, in depression.<sup>70</sup> Treating insomnia also improves depression (eg, Refs.<sup>53,64</sup>); however, it is unclear how and why: more research into the mechanisms by which treating insomnia improves mood is needed. Often, mediation analysis is used to study such mechanisms (eg, Ref.<sup>79</sup>). To do this successfully, the mediator should be measured during and after intervention but before the effects occur and the sample size should be substantial.<sup>97</sup> I-CBTi has made it possible to do large trials adequately powered to assess mediation. These studies suggest that improvement of insomnia symptoms is preceding the improvements in depression (eg, Refs.<sup>50,51</sup>). Recently, network approaches have been developed to investigate changes in specific symptoms, instead of full questionnaires only. This new tool called Network Intervention Analysis (NIA<sup>98</sup>) can be used to study trial data using specific symptoms. This approach demonstrated that depression symptoms clear up *after* specific insomnia symptoms.<sup>98</sup> NIA could be used on other datasets in the field of I-CBTi to provide more insight into working mechanisms and hence into optimizing treatment response in patients with insomnia.

**PERSONALIZING INTERNET-DELIVERED COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA**

In psychotherapy, an important question is: what works for whom? As discussed previously, more knowledge on the working mechanisms of I-CBTi will likely lead to better treatments, but efficacy of the treatment also could depend on person-specific factors. It has been suggested that online CBT effects on anxiety and depression are moderated by age (older people reporting fewer beneficial effects) but not by other “person, problem, program, or provider characteristics.”<sup>82</sup> For insomnia treatment, research by Cheng and colleagues<sup>67</sup> showed that I-CBTi effectively reduces symptoms across a wide range of demographic characteristics. Their large study was the first to identify different potential factors influencing the scope of treatment benefit, such as age, gender, socioeconomic status, and baseline severity, but also comorbidities in mental and physical health. They did not find any demographic variables to be associated with treatment efficacy and concluded that I-CBTi can be successfully offered

to a wide and varied range of persons with insomnia complaints.<sup>67</sup> Luik and colleagues<sup>83</sup> suggested in their review that being younger and more highly educated improves one's chances of success.<sup>99,100</sup> They also reported on clinical predictors of treatment success. The limited available research suggests that comorbid sleep disorders other than insomnia, a higher initial sleep efficiency, lower baseline severity of insomnia, and longer total sleep time at the start of treatment may put a person at risk of improving little or not at all from I-CBTI.<sup>83</sup>

I-CBTI does not work for everyone suffering from insomnia.<sup>75</sup> The insomnia subtypes introduced by Blanken and colleagues<sup>90</sup> might offer a promising approach for tailoring treatment. Their 5 subtypes are as follows: (1) highly distressed; (2) moderately distressed, intact response to pleasurable emotions; (3) moderately distressed, weak response to pleasurable emotions; (4) low distress, low reactivity to environment and life events; and (5) low distress and high reactivity to environment and life events.<sup>90</sup> These stable subtypes have been shown to differ in biologically based traits and life history and treatment response.<sup>90</sup> Future research should focus on whether different insomnia treatments have different effects on the subtypes; that is, their clinical relevance. Specific subtypes may be present that will or will not respond well to I-CBTI. For example, a person whose subtype is particularly characterized by high presleep arousal might benefit more from mindfulness or acceptance-based techniques than from cognitive therapies.

## COST-EFFECTIVENESS

Insomnia is a problem accompanied by substantial health care and societal costs, the latter for example, due to productivity loss and absence from work.<sup>7</sup> Treatment of insomnia could therefore potentially lead to large cost savings. Unfortunately, the cost-effectiveness of I-CBTI (or CBTI in general), has not been studied often. At least 3 studies have examined the cost-effectiveness of CBTI. These studies seem to suggest that the treatment is indeed cost-effective when offered in a face-to-face format,<sup>101</sup> to employees in online format,<sup>44</sup> and to adolescents online or in group format.<sup>102</sup> A pragmatic randomized controlled trial is currently under way studying whether I-CBTI can be offered cost-effectively in the general practice.<sup>103</sup>

## IMPLEMENTATION

I-CBTI has several advantages that could facilitate implementation. It can be administered without

scheduling appointments, and no travel time is required. This makes it suitable for those living remotely or with reduced mobility, limited time or busy schedules, and for those experiencing stigma preventing them from seeking face-to-face help. In addition, I-CBTI reduces waiting lists because much less resource is needed. However, online therapy also has some disadvantages that could impede implementation. A person has to invest a significant amount of time, which might require more self-discipline without face-to-face contact. In addition, people may have particular concerns about data privacy when data are shared online.<sup>104</sup> This makes it critical that programs adhere to respective regulations concerning data security. Also, not all persons suffering from insomnia may want online therapy: some insist on seeing a therapist, but equally some will prefer online treatment. Another concern might be related to personal safety. It may be preferable to keep a health care professional involved when a patient with insomnia is taking any online treatment. Automated systems can have algorithms to deal with certain safety issues. For example, when a program detects certain problems in the patient's answers (eg, suicide risk), patients could be automatically advised to contact their GP or health care professional, or a professional could be alerted to contact the patient automatically.

After determining effectiveness, working mechanisms, and costs associated with the treatment, the next big question is how best to implement online insomnia treatments. Whether or not a treatment is offered with or without support is an important factor in the implementation process. Accessible online treatments that are offered without human feedback are very scalable. Currently, a number of online programs can be freely purchased, but most programs are provided via research programs, health insurance programs, or at a (primary or secondary) care facility. Ideally, the guidelines recommending CBT for insomnia<sup>31,32</sup> should facilitate easy access to reimbursed treatment for diagnosed patients seeking help. Siversten and Nordgreen<sup>105</sup> have advised implementation of a varied range of modalities in which CBTI is offered, ranging from self-help material to online treatment to face-to-face conversations. Face-to-face therapy should then, due to scarcity of therapists, be provided only to those patients not helped (enough) through any of the other methods; that is, using a stepped-care approach.<sup>105</sup>

## SUMMARY

There is ample evidence that I-CBTI is an effective treatment for those suffering from insomnia. This

enables tailoring precision medicine to individual needs and characteristics. I-CBTi has the potential to play an important role in precision medicine because of its flexibility, accessibility, low costs, and multiple tailoring options. More research is needed looking into the moderators, mediators, and working mechanisms underlying the effects of I-CBTi on insomnia and other psychopathology to reach this potential. Then, we can offer efficacious treatment to those currently not benefiting from I-CBTi treatment, for reasons yet unknown. This would provide a strong incentive to implement I-CBTi on a larger scale, reaching more people, offering a true and perhaps preferable alternative to pharmacotherapy.

## RESEARCH AGENDA

We suggest the following gaps in current research should be addressed:

1. Establishing patient characteristics influencing treatment success to facilitate a precision medicine approach.
2. Further specifying (sub)types of patients with insomnia and identifying optimal ways to offer subtype-specific treatment in a stepped-care and cost-effective manner.
3. Determining the working mechanisms of I-CBTi to be able to specifically target these in treatment.

## REFERENCES

1. APA committee. Diagnostic and statistical manual of mental disorders, 5th edition: DSM-5. Washington, DC: American Psychiatric Association; 2013.
2. Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Med Rev* 2002;6:97–111.
3. Morin CM, Bélanger L, LeBlanc M, et al. The natural history of insomnia: a population-based 3-year longitudinal study. *Arch Intern Med* 2009;169:447–53.
4. Baglioni C, Riemann D. Is chronic insomnia a precursor to major depression? Epidemiological and biological findings. *Curr Psychiatry Rep* 2012;14:511–8.
5. Suh S, Kim H, Yang HC, et al. Longitudinal course of depression scores with and without insomnia in non-depressed individuals: a 6-year follow-up longitudinal study in a Korean cohort. *Sleep* 2013;36:369–76.
6. Olfson M, Wall M, Liu SM, et al. Insomnia and impaired quality of life in the United States. *J Clin Psychiatry* 2018;79.
7. Daley M, Morin CM, LeBlanc M, et al. The economic burden of insomnia: direct and indirect costs for individuals with insomnia syndrome, insomnia symptoms, and good sleepers. *Sleep* 2009;32:55–64.
8. Kessler RC, Berglund PA, Coulouvrat C, et al. Insomnia and the performance of US workers: results from the America insomnia survey. *Sleep* 2011;34:1161–71.
9. Hoebert JM, Souverein PC, Mantel-Teeuwisse AK, et al. Reimbursement restriction and moderate decrease in benzodiazepine use in general practice. *Ann Fam Med* 2012;10:42–9.
10. Bertisch SM, Herzig SJ, Winkelman JW, et al. National use of prescription medications for insomnia: NHANES 1999–2010. *Sleep* 2014;37:343–9.
11. Glass J, Lanctôt KL, Herrmann N, et al. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. *BMJ* 2005;331:1169.
12. Buscemi N, Vandermeer B, Friesen C, et al. The efficacy and safety of drug treatments for chronic insomnia in adults: a meta-analysis of RCTs. *J Gen Intern Med* 2007;22:1335.
13. Manconi M, Ferri R, Miano S, et al. Sleep architecture in insomniacs with severe benzodiazepine abuse. *Clin Neurophysiol* 2017;128:875–81.
14. Hintze JP, Edinger JD. Hypnotic discontinuation in chronic insomnia. *Sleep Med Clin* 2018;13:263–70.
15. Holbrook AM, Crowther R, Lotter A, et al. Meta-analysis of benzodiazepine use in the treatment of insomnia. *Can Med Assoc J* 2000;162:225–33.
16. Smith MT, Perlis ML, Park A, et al. Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *Am J Psychiatry* 2002;159:5–11.
17. Riemann D, Perlis ML. The treatments of chronic insomnia: a review of benzodiazepine receptor agonists and psychological and behavioral therapies. *Sleep Med Clin* 2009;13:205–14.
18. Everitt H, Baldwin D, Stuart B, et al. Antidepressants for insomnia in adults. New Jersey: Cochrane Library; 2018.
19. Kyle SD, Miller CB, Rogers Z, et al. Sleep restriction therapy for insomnia is associated with reduced objective total sleep time, increased daytime somnolence, and objectively impaired vigilance: implications for the clinical management of insomnia disorder. *Sleep* 2014;37:229–37.
20. American Academy of Sleep Medicine. International classification of sleep disorders. Diagnostic and coding manual 2005;2:51–5.
21. Morin CM, Espie CA. *Insomnia: a clinical guide to assessment and treatment*. New York: Springer Science & Business; 2007.
22. Murtagh DR, Greenwood KM. Identifying effective psychological treatments for insomnia: a meta-analysis. *J Consult Clin Psychol* 1995;63:79.
23. Edinger JD, Wohlgemuth WK. The significance and management of persistent primary insomnia: the

- past, present and future of behavioral insomnia therapies. *Sleep Med Rev* 1999;3:101–8.
24. Harvey AG, Tang NK. Cognitive behaviour therapy for primary insomnia: can we rest yet? *Sleep Med Rev* 2003;7:237–62.
  25. Montgomery P, Dennis J. A systematic review of non-pharmacological therapies for sleep problems in later life. *Sleep Med Rev* 2004;8:47–62.
  26. Morin CM, Bootzin RR, Buysse DJ, et al. Psychological and behavioral treatment of insomnia: update of the recent evidence (1998–2004). *Sleep* 2006;29:1398–414.
  27. Siebern AT, Suh S, Nowakowski S. Non-pharmacological treatment of insomnia. *Neurotherapeutics* 2012;9:717–27.
  28. Trauer JM, Qian MY, Doyle JS, et al. Cognitive behavioral therapy for chronic insomnia: a systematic review and meta-analysis. *Ann Intern Med* 2015;163:191–204.
  29. Van Straten A, van der Zweerde T, Kleiboer A, et al. Cognitive and behavioral therapies in the treatment of insomnia: a meta-analysis. *Sleep Med Rev* 2018;38:3–16.
  30. Van der Zweerde T, Bisdounis L, Kyle SD, et al. Cognitive behavioral therapy for insomnia: a meta-analysis of long-term effects in controlled studies. Under review.
  31. Riemann D, Baglioni C, Bassetti C, et al. European guideline for the diagnosis and treatment of insomnia. *J Sleep Res* 2017;26:675–700.
  32. Qaseem A, Kansagara D, Forciea MA, et al. Management of chronic insomnia disorder in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2016;165:125–33.
  33. Morin CM, LeBlanc M, Daley M, et al. Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. *Sleep Med* 2006;7:123–30.
  34. Everitt H, McDermott L, Leydon G, et al. GPs' management strategies for patients with insomnia: a survey and qualitative interview study. *Br J Gen Pract* 2014;64:112–9.
  35. Suzuki E, Tsuchiya M, Hirokawa K, et al. Evaluation of an Internet-based self-help program for better quality of sleep among Japanese workers: a randomized controlled trial. *J Occup Health* 2008;50:387–99.
  36. Blom K, Tillgren HT, Wiklund T, et al. Internet- vs. group-delivered cognitive behavior therapy for insomnia: a randomized controlled non-inferiority trial. *Behav Res Ther* 2015;70:47–55.
  37. Ström L, Pettersson R, Andersson G. Internet-based treatment for insomnia: a controlled evaluation. *J Consult Clin Psychol* 2004;72:113.
  38. Vincent N, Lewycky S. Logging on for better sleep: RCT of the effectiveness of online treatment for insomnia. *Sleep* 2009;32:807–15.
  39. Espie CA, Kyle SD, Williams C, et al. A randomized, placebo-controlled trial of online cognitive behavioral therapy for chronic insomnia disorder delivered via an automated media-rich web application. *Sleep* 2012;35:769–81.
  40. Lancee J, van den Bout J, van Straten A, et al. Internet-delivered or mailed self-help treatment for insomnia? A randomized waiting-list controlled trial. *Behav Res Ther* 2012;50:22–9.
  41. Ho FYY, Chung KF, Yeung WF, et al. Weekly brief phone support in self-help cognitive behavioral therapy for insomnia disorder: relevance to adherence and efficacy. *Behav Res Ther* 2014;63:147–56.
  42. Van Straten A, Emmelkamp J, De Wit J, et al. Guided Internet-delivered cognitive behavioural treatment for insomnia: a randomized trial. *Psychol Med* 2014;44:1521–32.
  43. Lancee J, Eisma MC, van Straten A, et al. Sleep-related safety behaviors and dysfunctional beliefs mediate the efficacy of online CBT for insomnia: a randomized controlled trial. *Cogn Behav Ther* 2015;44:406–22.
  44. Thiart H, Ebert DD, Lehr D, et al. Internet-based cognitive behavioral therapy for insomnia: a health economic evaluation. *Sleep* 2016;39:1769.
  45. Bernstein AM, Allexandre D, Bena J, et al. “Go! to sleep”: a web-based therapy for insomnia. *Telemed J E Health* 2017;23:590–9.
  46. Hagatun S, Vedaa Ø, Nordgreen T, et al. The short-term efficacy of an unguided Internet-based cognitive-behavioral therapy for insomnia: a randomized controlled trial with a six-month nonrandomized follow-up. *Behav Sleep Med* 2019;17(2):137–55.
  47. Horsch CH, Lancee J, Griffioen-Both F, et al. Mobile phone-delivered cognitive behavioral therapy for insomnia: a randomized waitlist controlled trial. *J Med Internet Res* 2017;9. <https://doi.org/10.2196/jmir.6524>.
  48. Ritterband LM, Thorndike FP, Ingersoll KS, et al. Effect of a web-based cognitive behavior therapy for insomnia intervention with 1-year follow-up: a randomized clinical trial. *JAMA Psychiatry* 2017;74:68–75.
  49. de Bruin EJ, Bögels SM, Oort FJ, et al. Efficacy of cognitive behavioral therapy for insomnia in adolescents: a randomized controlled trial with Internet therapy, group therapy and a waiting list condition. *Sleep* 2015;38:1913–26.
  50. Espie CA, Emsley R, Kyle SD, et al. Effect of digital cognitive behavioral therapy for insomnia on health, psychological well-being, and sleep-related quality of life: a randomized clinical trial. *JAMA Psychiatry* 2018. <https://doi.org/10.1001/jamapsychiatry.2018.2745>.

51. Freeman D, Sheaves B, Goodwin GM, et al. The effects of improving sleep on mental health (OASIS): a randomised controlled trial with mediation analysis. *Lancet Psychiatry* 2017;4:749–58.
52. Lancee J, van Straten A, Morina N, et al. Guided online or face-to-face cognitive behavioral treatment for insomnia: a randomized wait-list controlled trial. *Sleep* 2016;39:183–91.
53. Van der Zweerde T, Van Straten A, Efting M, et al. Does online insomnia treatment reduce depressive symptoms? A randomized controlled trial in individuals with both insomnia and depressive symptoms. *Psychol Med* 2019;49(3):501–9.
54. Kaldo V, Jernelöv S, Blom K, et al. Guided Internet cognitive behavioral therapy for insomnia compared to a control treatment—a randomized trial. *Behav Res Ther* 2015;71:90–100.
55. Thiart H, Lehr D, Ebert DD, et al. Log in and breathe out: Internet-based recovery training for sleepless employees with work-related strain—results of a randomized controlled trial. *Scand J Work Environ Health* 2015;41:164–74.
56. Chow PI, Ingersoll KS, Thorndike FP, et al. Cognitive mechanisms of sleep outcomes in a randomized clinical trial of Internet-based cognitive behavioral therapy for insomnia. *Sleep Med* 2018;47:77–85.
57. Blom K, Jernelöv S, Kraepelien M, et al. Internet treatment addressing either insomnia or depression, for patients with both diagnoses: a randomized trial. *Sleep* 2015;38:267–77.
58. Spek V, Cuijpers P, Nyklicek I, et al. Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. *Psychol Med* 2007;33:319–28.
59. Lancee J, van den Bout J, Sorbi MJ, et al. Motivational support provided via email improves the effectiveness of Internet-delivered self-help treatment for insomnia: a randomized trial. *Behav Res Ther* 2013;51:797–805.
60. Jernelöv S, Lekander M, Blom K, et al. Efficacy of a behavioral self-help treatment with or without therapist guidance for co-morbid and primary insomnia—a randomized controlled trial. *BMC Psychiatry* 2012;12:5.
61. Zachariae R, Lyby MS, Ritterband LM, et al. Efficacy of Internet-delivered cognitive-behavioral therapy for insomnia—a systematic review and meta-analysis of randomized controlled trials. *Sleep Med Rev* 2016;30:1–10.
62. Andersson G, Cuijpers P. Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. *Cogn Behav Ther* 2009;38:196–205.
63. Ritterband LM, Thorndike FP, Gonder-Frederick LA, et al. Efficacy of an Internet-based behavioral intervention for adults with insomnia. *Arch Gen Psychiatry* 2009;66:692–8.
64. Christensen H, Batterham PJ, Gosling JA, et al. Effectiveness of an online insomnia program (SHUTi) for prevention of depressive episodes (the GoodNight Study): a randomised controlled trial. *Lancet Psychiatry* 2016;3:333–41.
65. Bostock S, Luik AI, Espie CA. Sleep and productivity benefits of digital cognitive behavioral therapy for insomnia: a randomized controlled trial conducted in the workplace environment. *J Occup Environ Med* 2016;58:683–9.
66. Barnes CM, Miller JA, Bostock S. Helping employees sleep well: effects of cognitive behavioral therapy for insomnia on work outcomes. *J Appl Psychol* 2017;102:104.
67. Cheng P, Luik AI, Fellman-Couture C, et al. Efficacy of digital CBT for insomnia to reduce depression across demographic groups: a randomized trial. *Psychol Med* 2019;49:491–500.
68. Pigeon WR, Bishop TM, Krueger KM. Insomnia as a precipitating factor in new onset mental illness: a systematic review of recent findings. *Curr Psychiatry Rep* 2017;19:44.
69. Li MJ, Kechter A, Olmstead RE, et al. Sleep and mood in older adults: coinciding changes in insomnia and depression symptoms. *Int Psychogeriatr* 2018;30:431–5.
70. Carney CE, Segal ZV, Edinger JD, et al. A comparison of rates of residual insomnia symptoms following pharmacotherapy or cognitive-behavioral therapy for major depressive disorder. *J Clin Psychiatry* 2007;68:254–60.
71. Ballesio A, Aquino MRJV, Feige B, et al. The effectiveness of behavioural and cognitive behavioural therapies for insomnia on depressive and fatigue symptoms: a systematic review and network meta-analysis. *Sleep Med Rev* 2017;37:114–29.
72. Gebara MA, Siripong N, DiNapoli EA, et al. Effect of insomnia treatments on depression: a systematic review and meta-analysis. *Depress Anxiety* 2018;35:717–31.
73. Ye YY, Zhang YF, Chen J, et al. Internet-based cognitive behavioral therapy for insomnia (ICBT-i) improves comorbid anxiety and depression—a meta-analysis of randomized controlled trials. *PLoS One* 2015;10:e0142258.
74. Kyle SD, Crawford MR, Morgan K, et al. The Glasgow Sleep Impact Index (GSII): a novel patient-centered measure for assessing sleep-related quality of life impairment in insomnia disorder. *Sleep Med* 2013;14:493–501.
75. Morin CM, Benca R. Chronic insomnia. *Lancet* 2012;379:1129–41.
76. Okajima I, Nakajima S, Ochi M, et al. Reducing dysfunctional beliefs about sleep does not significantly improve insomnia in cognitive behavioral therapy. *PLoS One* 2014;9:e102565.



77. Espie CA, Kyle SD, Miller CB, et al. Attribution, cognition and psychopathology in persistent insomnia disorder: outcome and mediation analysis from a randomized placebo-controlled trial of online cognitive behavioural therapy. *Sleep Med* 2014;15:913–7.
78. Harvey AG, Dong L, Bélanger L, et al. Mediators and treatment matching in behavior therapy, cognitive therapy and cognitive behavior therapy for chronic insomnia. *J Consult Clin Psychol* 2017; 85:975.
79. Norell-Clarke A, Tillfors M, Jansson-Fröjmark M, et al. How does cognitive behavioral therapy for insomnia work? An investigation of cognitive processes and time in bed as outcomes and mediators in a sample with insomnia and depressive symptomatology. *Int J Cogn Ther* 2017;10:304–29.
80. Lancee J, Eftting M, Van der Zweerde T, et al. Cognitive processes mediate the effects of insomnia treatment: evidence from a randomized wait-list controlled trial. *Sleep Med* 2019;54:86–93.
81. Harvey AG. A cognitive model of insomnia. *Behav Res Ther* 2002;40:869–93.
82. Grist R, Cavanagh K. Computerised cognitive behavioural therapy for common mental health disorders, what works, for whom under what circumstances? A systematic review and meta-analysis. *J Contemp Psychother* 2013;43: 243–51.
83. Espie CA, Bostock S, Kyle SD, et al. Who benefits from online CBT for insomnia? Factors associated with change in sleep efficiency in a large online treatment cohort. *Sleep* 2014;37:A205.
84. Yeung WF, Chung KF, Ho FYY, et al. Predictors of dropout from Internet-based self-help cognitive behavioral therapy for insomnia. *Behav Res Ther* 2015;73:19–24.
85. Bathgate CJ, Edinger J, Krystal AD. Insomnia patients with objective short sleep duration have a blunted response to cognitive behavioral therapy for insomnia. *Sleep* 2017;40.
86. Blom K, Jernelöv S, Lindefors N, et al. Facilitating and hindering factors in Internet-delivered treatment for insomnia and depression. *Internet Interv* 2016;4:51–60.
87. Dong L, Soehner AM, Bélanger L, et al. Treatment agreement, adherence, and outcome in cognitive behavioral treatments for insomnia. *J Consult Clin Psychol* 2018;86:294.
88. Webb TL, Joseph J, Yardley L, et al. Using the Internet to promote health behavior change: a systematic review and meta-analysis of the impact of theoretical basis, use of behavior change techniques, and mode of delivery on efficacy. *J Med Internet Res* 2010;12.
89. Wu JQ, Appleman ER, Salazar RD, et al. Cognitive behavioral therapy for insomnia comorbid with psychiatric and medical conditions: a meta-analysis. *JAMA Intern Med* 2015;175:1461–72.
90. Blanken TF, Benjamins JS, Borsboom D, et al. Robust insomnia disorder subtypes revealed by non-sleep-related traits and life history. *Lancet Psychiatry* 2019;6(2):151–63.
91. Castelnovo A, Ferri R, Punjabi NM, et al. The paradox of paradoxical insomnia: a theoretical review towards a unifying evidence-based definition. *Sleep Med Rev* 2018;44:70–82.
92. Perlis ML, Giles DE, Mendelson WB, et al. Psychophysiological insomnia: the behavioural model and a neurocognitive perspective. *J Sleep Res* 1997;6: 179–88.
93. Riemann D, Spiegelhalter K, Feige B, et al. The hyperarousal model of insomnia: a review of the concept and its evidence. *Sleep Med Rev* 2010;14:19–31.
94. Schwartz DR, Carney CE. Mediators of cognitive-behavioral therapy for insomnia: a review of randomized controlled trials and secondary analysis studies. *Clin Psychol Rev* 2012;32:664–75.
95. Sunnhed R, Jansson-Fröjmark M. Are changes in worry associated with treatment response in cognitive behavioral therapy for insomnia? *Cogn Behav Ther* 2014;43:1–11.
96. Okuji Y, Matsuura M, Kawasaki N, et al. Prevalence of insomnia in various psychiatric diagnostic categories. *Psychiatry Clin Neurosci* 2002;56:239–40.
97. Kazdin AE. Understanding how and why psychotherapy leads to change. *Psychother Res* 2009; 19:418–28.
98. Blanken TF, Van der Zweerde T, Van Straten A, et al. Introducing Network Intervention Analysis to investigate sequential, symptom-specific treatment effects: a demonstration in co-occurring insomnia and depression. *Psychother Psychosom* 2019; 88(1):52–4.
99. Vincent N, Walsh K, Lewycky S. Determinants of success for computerized cognitive behavior therapy: examination of an insomnia program. *Behav Sleep Med* 2013;11:328–42.
100. Espie CA, Bostock S, Kyle SD, et al. Who benefits from online CBT for insomnia? Factors associated with change in sleep efficiency in a large online treatment cohort. *Sleep* 2014;37:A205.
101. Watanabe N, Furukawa TA, Shimodera S, et al. Cost-effectiveness of cognitive behavioral therapy for insomnia comorbid with depression: analysis of a randomized controlled trial. *Psychiatry Clin Neurosci* 2015;69:335–43.
102. De Bruin EJ, van Steensel FJ, Meijer AM. Cost-effectiveness of group and Internet cognitive behavioral therapy for insomnia in adolescents: results from a randomized controlled trial. *Sleep* 2016;39:1571–81.
103. Van der Zweerde T, Lancee J, Slottje P, et al. Cost-effectiveness of i-Sleep, a guided online CBT



- intervention, for patients with insomnia in general practice: protocol of a pragmatic randomized controlled trial. *BMC Psychiatry* 2016;85.
104. Coulson NS, Smedley R, Bostock S, et al. The pros and cons of getting engaged in an online social community embedded within digital cognitive behavioral therapy for insomnia: survey among users. *J Med Internet Res* 2016;18. <https://doi.org/10.2196/jmir.5654>.
105. Siversten B, Vedaa Ø, Nordgreen T. The future of insomnia treatment—the challenge of implementation. *Sleep* 2013;36:303–4.